

# In Vitro Study Concerning the Efficiency of the Frequency-Doubled Double-Pulse Neodymium:YAG Laser (FREDDY) for Lithotripsy of Calculi in the Urinary Tract

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**Background and Objectives:** In a preclinical study we have tested both in vitro and in vivo, a new type of pulsed solid-state laser system that has not been applied in urology so far and has been developed for optimized intracorporal lithotripsy of biliary, salivary, and urinary calculi.

**Study Design/Materials and Methods:** Sixty one calculi from the human urinary tract were split in vitro into fragments with a remaining particle size of  $\leq 2$  mm using the prototype of a short-pulsed passively Q-switched and frequency-doubled double-pulse Neodymium:YAG laser. In a supplementary animal test, the bladder mucosa of five rabbits was directly exposed to a highly rated laser beam to be able to assess the tissue lesion potential of the system.

**Results:** All the 61 urinary calculi with different composition were successfully split in vitro within a short period of time ( $2.5 \pm 4.6$  minutes). During histopathologic examination of the exposed bladder walls of the rabbits only a small tissue lesion potential with urothelium changes exclusively at the surface was ascertained.

**Conclusion:** The high degree of fragmentation efficiency, the purchase and maintenance costs, which due to its design are substantially lower in comparison to other laser lithotriptors, and the high degree of safety during application make this new laser a real alternative not only to the present laser lithotripsy systems but also to common ballistic lithotriptors. *Lasers Surg. Med.* 25:38–42, 1999. © 1999 Wiley-Liss, Inc.

**Key words:** laser lithotripsy; urinary calculi; solid-state laser; frequency-doubled double-pulse Neodymium:YAG laser

## INTRODUCTION

The subject of the examination was the prototype of a new Neodymium:YAG laser. This is a short-pulsed Q-switched frequency-doubled double-pulse Neodymium:YAG-solid-state laser, which in addition to enabling the emission of very long pulses in the range of micro-seconds (1.0–1.4  $\mu$ s) due to its new resonator design also makes it possible to produce a very high pulse intensity as

well as shock wave intensity due to the partial frequency doubling of the infrared ray ( $\lambda; = 1,064$

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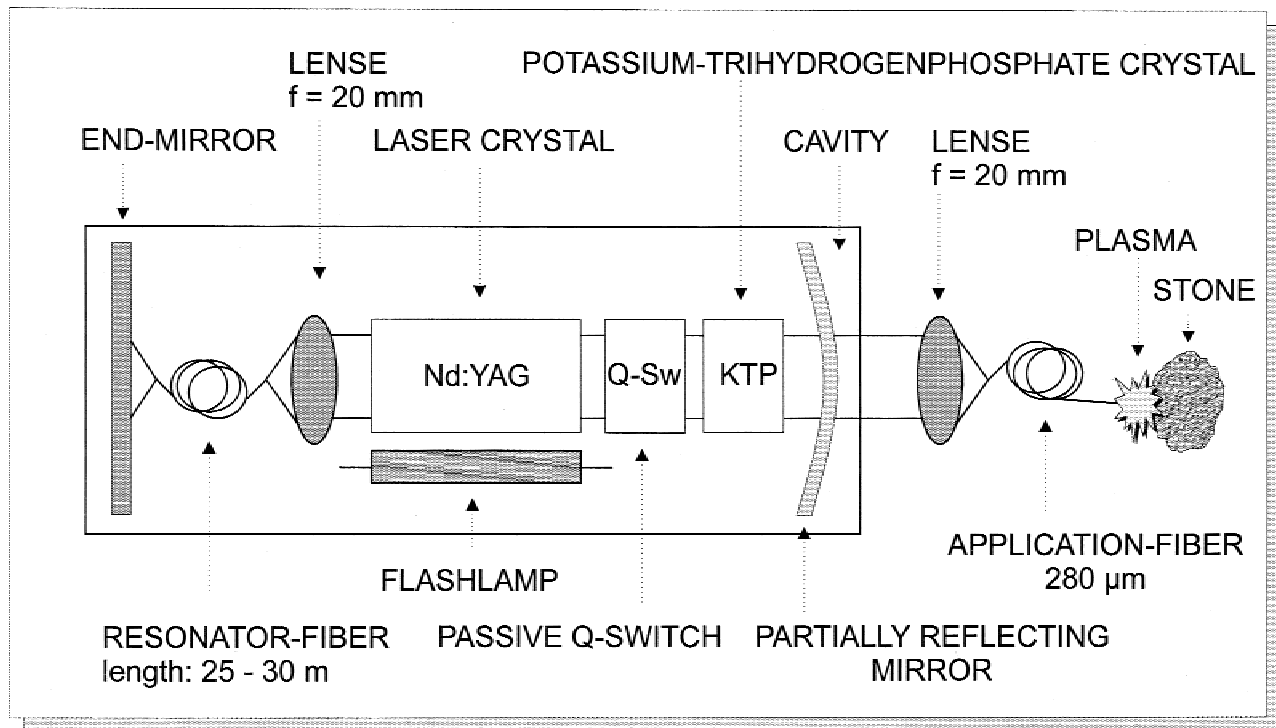


Fig. 1. FREDDY technology: The laser-resonator technical set up of the LITHON, showing resonator configuration of the Q-switched solid-state laser with fiber resonator and KTP-crystal.

nm) into the green range ( $\lambda = 532$  nm) [1]. This laser system combines the advantages of solid-state lasers with those of dye lasers, with the purchase and the maintenance costs being only approximately 30% of present laser systems [1]. As a result, particularly in present times this system is to be regarded as a direct alternative not only to the present intracorporeal laser lithotripsy systems but also to the presently established ballistic lithotriptors such as Lithoclast. For these reasons, it was practical to test the efficiency and safety of this new laser lithotripsy system in a preclinical study to assess its clinical application in urology in practice.

## MATERIALS AND METHODS

### Laser System

This system refers to the prototype of a new laser, using the patented FREDDY technology, i.e., short-pulsed passively Q-switched and frequency-doubled double-pulse Neodymium:YAG. The laser has been given the company name "LITHON" by the CLYXON company (Berlin, Germany, [www.CLYXON.com](http://www.CLYXON.com)).

The system comprises an internal water

cooling circuit with a water-air heat exchanger and can be connected to the conventional single phase power supply (110 V...220 V, 10 A). Thus, the system does not require connection to an external water supply or to a heavy power supply as is the case with present systems. This circumstance and also the fact that it has small dimensions make the system highly mobile and easy to handle. By integrating a 25–30-m long all silica fiber into the resonator of the laser the pulse duration of the Q-switched Nd:YAG laser, which normally is in the range of nanoseconds could be extended into the range of microseconds (1,0–1,4  $\mu$ s) [2] (Fig. 1). By an intracavity KTP-(potassium trihydrogenphosphate) crystal a fraction of about 20% of the laser power of the fundamental laser wavelength is frequency doubled ( $\lambda = 1,064$  nm) into the green second harmonic ( $\lambda = 532$  nm). This results in the formation of a so-called "double pulse" in which both wavelengths are combined as individual pulses and synchronized in time [3] (Fig.2). After the plasma has been induced at the surface of the calculus by the share of green in the pulse, the plasma that is a so-called "black absorber" and is thus able to absorb a maximum amount of incident rays will be energetically pumped by the accompanying infrared pulse rich

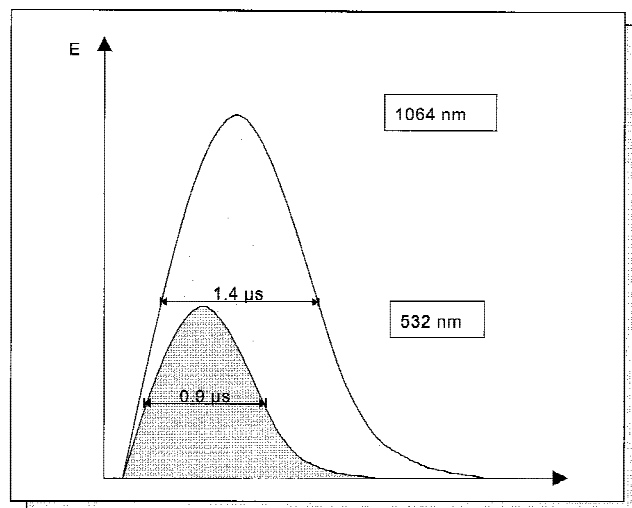


Fig. 2. FREDDY technology: The double-pulse principle of "double pulse" generated by the LITHON, showing both wavelengths  $\lambda = 1,064$  nm and  $\lambda = 532$  nm.

in energy ("Plasma shielding") [2,3]. The result is increased pulse efficiency.

For the experiments an application energy of 90 mJ at a pulse repetition rate of 10 Hz was chosen. The laser double pulses were guided to the stone via a highly flexible step-index all silica fiber with a tefzel or polyamide coating and a core diameter of 280  $\mu$ m. Before re-applying the laser beam to a new stone, the laser energy adjusted was controlled by means of an external energy control device (ED 200, GenTech, Québec, Canada). During energy application the fiber was always directly in contact with the calculus. Before every stone splitting the distal end of the fiber was freshly broken and stripped and then the fiber cross-section was checked for regular geometry by means of the pilot ray. It was not necessary to change the fiber before every new application or during its use due to the very low degree of fiber tip consumption.

#### MATERIAL OF THE CALCULI AND TEST SET-UP

First the maximum diameter and the weight of 61 calculi or calculi fragments were determined. They originated from the human urinary tract, were of different mineralogic composition, and were taken from previous transurethral or percutaneous lithotripsies or removals of calculi.

The laser lithotripsy of the urinary calculus was carried out in a glass cone and was continued until the stone was washed out through the discharge pipe with a diameter of 2 mm. Splitting the calculus sample into residual particles with a

TABLE 1. Stone Types and Fragmentation Rate

Stone category	No.	Fragmentation rate (mg/minute)				
		Mean	Std D	Median	Min	Max
Whewellit	25	160.7	143.7	132.2	3	640
Uric acid	21	59.4	53.1	43.9	5	223
Apatit	10	112.9	80.0	112.1	15	209
Weddellit	3	198.5	99.7	194.7	101	300
Brushit	1	7.9	—	—	—	—
Struvit	1	61.6	—	—	—	—
Total	61	115.7	114.1	77.0	3	640

size of  $\leq 2$  mm was therefore regarded as complete disintegration. Lithotripsy was carried out under a fluid level that was kept at a constant level by continuously supplying isotonic salt solution. The discharged rinsing fluid was collected under the glass cone. After complete fragmentation of the test sample the eluate was subject to the process of microfiltration. The resulting fragment material was dried and its chemical composition was analysed using the process of infrared spectrometry. Six different calculus compositions were determined (Table 1).

#### TISSUE LESION

The examinations concerning the potential of soft tissue damage of the new laser system were carried out in cooperation with the First Medical Clinic and the Department for Clinical Pathology of the Friedrich-Alexander-Universität in Erlangen-Nürnberg during an approved project with animal testing.

For this purpose, the bladder wall of the opened urinary bladders of five narcotized laboratory rabbits were subjected to laser treatment with 2,000 pulses and 90 mJ energy. The laser energy was applied to the mucosa in the worst possible, i.e., constant direct contact of the fiber tip and holding the fiber perpendicular to the mucosa surface.

The rabbits were killed after the exposition and the areas where the laser hit the bladder wall were subject to a careful histopathologic examination. These areas were also examined under a light microscope by an experienced clinic pathologist for tissue lesions.

#### STATISTICAL EVALUATION

For a better assessment of the laser efficiency in clinical use, the laser pulses required for the complete fragmentation of calculus were related to the corresponding calculus weight in mg and to the corresponding calculus diameter in mm (referred to as fragmentation rate in the Results

TABLE 2. Statistical Evaluation of the Measurements

	Mean	Std D	Median	Min	Max
Weight of stones in mg	78.5	45.8	65.0	21.0	218.0
Max stone diameter in mm	6.2	1.5	6.1	3.8	10.5
Number of pulses	1491.0	2742.0	539.0	49.0	16,305.0
Pulses/mg	17.6	32.0	7.8	0.9	211.5
Pulses/mm	234.6	459.6	91.8	9.8	2,631.3
Net application time in minute	2.5	4.6	0.9	0.1	27.2
Fragmentations rate in mg/minute	115.7	114.1	77.0	3.0	640.0
Number of stones (n)	61				
Fragmentation effectivity	100%				

section). Moreover, the removal rate in calculus weight per time unit (mg/minute) was calculated from the individual values. In the table of results the corresponding calculated mean values are specified together with the standard deviations, the median values, the maxima, and minima. We used SPSS 8.0 for Windows to calculate the values.

## RESULTS

All 61 urinary calculi could be successfully fragmented into residual particles  $\leq 2$  mm. This corresponds to a fragmentation effectivity of 100%. Twenty five (41%) of the calculi examined were Whewellit-calculi, 21 (34.4%) uric acid calculi, 10 (16.4%) Apatitstones, 3 (5.0%) Weddellitstones, 1 (1.6%) was a Struvit-stone and 1 (1.6%) a Brushit-stone. The average calculus weight was  $78.49 \pm 45.46$  mg, the maximum calculus diameter was  $6.2 \pm 1.5$  mm.  $1,491 \pm 2,719$  pulses were required for fragmentation at a net application time of  $2.49 \pm 4.40$  minutes. The following parameters were calculated from these values: a removal rate of  $115.68 \pm 113.55$  mg/minute and a pulse rate of  $17.61 \pm 31.24$  pulse/mg or  $237.4 \pm 458.9$  pulse/mm (each with simple standard deviation) (Table 2).

A concentrated, selective laser beam applied to the urothelium of the rabbit only caused light mucosal oedemas with hyperaemia as well as light to medium-grade bleeding in the area of the lamina propria and a punctiform coagulation necrosis of the epithelial layer for all histologic preparations ( $n = 10$ ) even at maximum parameters of 90 mJ and 2,000 pulses. Neither lesions of the tunica muscularis nor perforations were found in any case.

## DISCUSSION

Being the subject of this study, the laser system LITHON proved that even many years after the introduction of laser lithotripsy in the urology-

cal calculus therapy, important improvements can still be made with new technical designs. A comparison between the presently obtained in vitro lithotripsy data and data earlier obtained by us with two other laser systems (Lasolith, Lithognost), which are already established in clinical treatment [4,5], revealed that in addition to its unachieved effectiveness LITHON has a fragmentation efficiency that was six times higher than in the conventional system. With this system it was possible to disintegrate every single one of the calculi, even those with a light surface or a high degree of calculi hardness, which was not always possible in previous studies with Lasolith. For the calculi disintegration this currently corresponds to a level required in clinical application.

Moreover, due to the highly flexible, very thin all silica fiber it is possible to use lasers both with rigid, modern semi-rigid, or flexible minimal-invasive ureteroscopes with low caliber (6–8 French) providing for high visibility since the rinsing tract will only be slightly narrowed. Being nowadays mainly used for reasons of cost, the ballistic Lithoclast-systems is, however, limited to the application in rigid or semi-rigid endoscopes. In addition, the visibility in the rinsing tract is impaired and as an undesired side effect, the calculus is often propelled into the pyelocalyceal system, which then requires a further calculus therapy such as ESWL. This disadvantage does not usually occur when using laser lithotripsy [6,7] or it is very rare. Furthermore, there is a much greater risk of perforation with the rigid endoscopy and the Lithoclast lithotripsy performed with a rigid metal probe compared to the minimal invasive laser lithotripsy [8]. Moreover, in the case of older patients with medium or large ureteral calculi a rigid ureteroscopy is often not possible in the first place whereas with the flexible ureteroscope and the fiber laser the calculus can be reached in almost every case.

With the design principle of the new laser lithotripter the purchase costs are substantially reduced compared to the present laser systems; the costs amount to ca. EURO 45,000, which may be only 30% of the previous costs. In addition, the fact that the system is largely maintenance-free and that the resulting regularly arising maintenance costs are very low may push these previous decisive disadvantages of laser lithotripsy compared to the ballistic lithotripsy to the background. As a result, in the future, smaller therapeutical units could add for example the ureteroscopic intracorporal laser lithotripsy to their range of calculus treatment as an efficient, safe, and minimal invasive unit thus substantially increasing the range. By combining interdisciplinary usability with great mobility, the LITHON is able to improve the cost-benefit-ratio even further.

For these reasons and due to the promising preclinical data we are currently carrying out a prospective randomized study with patients having ureteral calculi to compare the ureteroscopic laser lithotripsy performed with LITHON and the ballistic lithotripsy carried out with Lithoclast.

#### ACKNOWLEDGMENT

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